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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,072	02/03/2006	Cheol-Min Kim	50413/011001	2285

21559 7590 02/27/2009

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
02/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/567,072	KIM ET AL.	
	Examiner	Art Unit	
	AMANDA SHAW	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2008*.

2a)☒ This action is FINAL. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3, 7-8, 10-12, and 14* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,8 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed December 15, 2008. This action is made FINAL.

Claims 1-3 7-8, 10-12 and 14 are currently pending. Claims 14 has been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Claims 1 and 7 have been amended.

Withdrawn Rejections

2. The rejection made under 35 USC 112 2nd paragraph in section 2 of the Office Action of June 13, 2008 is withdrawn in view of amendments made to the claims.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand

alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the structural limitations of the oligonucleotides present on the microarray are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the claim language of "a microarray with target probes for detecting drug resistant HBV on a support" merely sets forth the intended use of the microarray, but does not limit the scope of the claims.

4. Claims 1-3 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor (US 2001/0053519 Pub 12/2001).

Regarding Claim 1 Fodor teaches an array comprising all possible nucleic acid sequences of any given length. For example a 10-mer array comprises all possible oligonucleotides containing 10 base positions (Col 17, lines 23-36). While Fodor does not specifically discuss probes for detecting point mutations at codons 528, 529, and 514 of domain B and at codons 552, 548, and 555 of domain C of the HBV DNA polymerase gene, it is a property of the array taught by Fodor that it would comprise probes capable of detecting these point mutations. In view of the comprising language in the claim the claimed microarray is not limited to probes that only detect these mutations. In the instant case a recitation of a new intended use (i.e. wherein said

microarray can be used to detect drug resistant HBV) for an old product (i.e. the microarray of Fodor) does not make a claim to that old product patentable. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

Regarding Claim 2 Fodor teaches a microarray on a support wherein the support is a gel (Col 2, lines 34-35).

Regarding Claim 3 Fodor teaches that the probes are oligonucleotides (abstract).

Regarding Claims 7-8 it is inherent that the microarray of Fodor would comprise negative control probes that have been prepared by substituting, inserting, or deleting at least one nucleotide sequence among the nucleotide sequences of the target probes not to be hybridized with a target product.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." In the present situation, the structural limitations of the oligonucleotides present on the microarray are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the claim language of "a microarray with target probes for detecting drug resistant HBV on a support" merely sets forth the intended use of the microarray, but does not limit the scope of the claims.

6. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor (US 2001/0053519 Pub 12/2001) in view of Kincaid (US 2003/0186310 Filed 4/2003)

The teachings of Fodor are presented above.

Regarding Claim 10 Fodor does not teach a microarray further comprising quality control probes labeled with a fluorescent material having a different excitation/emission wavelength from a fluorescent material used to label the target product. Regarding

Claim 11 Fodor does not teach quality control probes that have arbitrary sequences that have at least one nucleotide labeled with a fluorescent material. Regarding Claim 12 Fodor does not teach that the quality control probes is labeled with Cyanine 3 or Cyanine 5.

However Kincaid teaches control probes on a microarray. The control probes can be any known sequence of nucleic acid as long as they do not interfere with the hybridization of the target sample. Kincaid further teaches that the control probes are labeled with a fluorescent material that emits a signal that is distinguishable from any other signal that may be used on the array (para 0016). An example of a label that can be used is CY3 and CY5 (para 0076).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the microarray of Fodor by adding control probes as suggested by Kincaid. The use of control probes were conventional in the field of molecular biology at the time the invention was made and provide the advantage of allowing one to be able to monitor hybridization to determine if the probes on the microarray are working.

7. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vernet (Virus Research 2002) in view of Liu (Antiviral Chemistry and Chemotherapy 2002).

Regarding Claim 1 Vernet teaches that one potential application of DNA Chip technology is in the field of clinical virology and diagnostics, as, for example genotypic

resistance tests (page 69). Vernet further teaches that resistance mutations in the genome of HBV have been described in response to antiviral therapies (pages 70). Regarding Claim 2 Vernet teaches a microarray on a support wherein the support is glass or silica (page 65). Regarding Claim 3 Vernet teaches that the probes are oligonucleotides (page 65).

Vernet does not disclose probes for detecting point mutations at codons 528, 529, and 514 of domain B and at codons 552, 548, and 555 of domain C of the HBV DNA polymerase gene.

However Liu teaches that the point mutations at codons 528, 529, and 514 of domain B and at codons 552, 548, and 555 of domain C of the HBV DNA polymerase gene were well known in the art (see Table 2). Liu further teaches that the point mutations have been reported as drug resistant mutations. While Liu does not teach probes specific for each of these point mutations, it was well known in the art at the time the invention that probes designed for a specific mutation could be used in order to detect that mutation. Designing such probes is considered routine experimentation. Further the parameters and objectives involved in designing these probes were known. Thus the prior art is replete with guidance and information necessary to permit the ordinary artisan to design probes for the detection of the recited point mutations. Further, using the computer programs available an ordinary artisan would have had more than a reasonable expectation of success of making probes for detecting these mutations. Additionally one would have been motivated to put these probes onto a microarray for the benefit of being able to detect the presence or absence of these

mutations using microarray technology that overcomes the low sensitivity, the high cost and the long time result of existing tests based on culture and direct or indirect immunoassay detection (Vernet page 70).

8. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vernet (Virus Research 2002) in view of Liu (Antiviral Chemistry and Chemotherapy 2002) as applied to claim 1 and in further view of Anderson (US 2003/0040870 Pub 2/2003)

The teachings of Vernet and Liu are presented above.

Regarding Claims 7-8 the combined references does not teach a microarray further comprising negative control probes that have been prepared by substituting, inserting, or deleting at least one nucleotide sequence among the nucleotide sequences of the target probes not to be hybridized with a target product.

However Anderson teaches negative control probes. For single base changes (such as a SNP) one probe was made to be the complement of the wild type sequence, one probe was made to be the complement of the mutated sequence, and one probe was made to be the complement of a different mutation (para 0064). Thus Anderson teaches negative control probes that have been prepared by substituting, inserting, or deleting at least one nucleotide sequence among the nucleotide sequences of the target probes not to be hybridized with a target product.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the microarray of Vernet and Liu by

adding negative control probes as suggested by Anderson. The use of control probes were conventional in the field of molecular biology at the time the invention was made and provide the advantage of allowing one to be able to monitor hybridization to determine if the probes on the microarray are working.

9. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vernet (Virus Research 2002) in view of Liu (Antiviral Chemistry and Chemotherapy 2002) as applied to claim 1 and in further view of Kincaid (US 2003/0186310 Filed 4/2003).

The teachings of Vernet and Liu are presented above.

The combined references do not teach a microarray further comprising quality control probes labeled with a fluorescent material having a different excitation/emission wavelength from a fluorescent material used to label the target product. Regarding Claim 11 combined references do not teach quality control probes that have arbitrary sequences that have at least one nucleotide labeled with a fluorescent material. Regarding Claim 12 combined references do not teach that the quality control probes is labeled with Cyanine 3 or Cyanine 5.

However Kincaid teaches control probes on a microarray. The control probes can be any known sequence of nucleic acid as long as they do not interfere with the hybridization of the target sample. Kincaid further teaches that the control probes are labeled with a fluorescent material that emits a signal that is distinguishable from any

other signal that may be used on the array (para 0016). An example of a label that can be used is CY3 and CY5 (para 0076).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the microarray of Vernet and Liu by adding control probes as suggested by Kincaid. The use of control probes were conventional in the field of molecular biology at the time the invention was made and provide the advantage of allowing one to be able to monitor hybridization to determine if the probes on the microarray are working.

Response To Arguments

10. In the response filed December 15, 2008, the Applicants traversed the art rejections.

Regarding the rejection made under 35 USC 102(b) over Fodor the Applicants submit that according to the Examiners position any invention relating to microarrays with target probes having certain mutant sequences for specific useful detecting cannot be patented. With respect to the preamble the Applicants point out that the target probes are used for detecting drug resistant HBV on a support, which clearly limits the microarrays to those that include such probes and which are useful for such detection. In order to be useful for this purpose there must be some type of design or specification that allows identification of binding to the HBV related probes. The Applicants assert that this is not taught by Fodor. Further claim 1 has been amended to specify in the body of the claim that the claimed microarray can be used to detect drug resistant HBV.

This argument has been fully considered but is not persuasive. Microarrays may be patented when the probes on the array are structurally distinct from probes that are taught in the prior art. In the instant case the only structural requirement of the probes present on the claimed microarray is that the probes include point mutations at specific codons. Here the defining elements are just too broad. Again the recitation of a microarray with target probes for detecting drug resistant hepatitis B virus on a support has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Further it is noted that the Applicants have amended claim 1 so that the intended use is present in the body of the claim, however a recitation of intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. There is no reason why one of skill in the art could not use the array of Fodor to detect drug resistant HBV particularly since the mutations that are associated with drug resistant HBV were well known in the art as evidenced by Liu (Antiviral Chemistry and Chemotherapy 2002).

Regarding the rejection made under 35 USC 103 over Fodor in view of Kincaid the Applicants reiterate their arguments over Fodor and state that since neither Fodor nor Kincaid mention probes for use in detecting drug resistant HBV the references cannot support the rejection. Further the Applicants argue that Kincaid discloses that the control probes comprise a sequence of nucleic acids unique to the control probe, whereas the quality control probes of the present invention may have the same sequence as the target probes or arbitrary sequences as specified in claim 11. In addition they argue that the control probes of Kincaid act as a stilt whereas the control probes of the present claims do not extend the target probes but rather are mixed with the target probes. Finally Applicants state that the control probes of Kincaid also need control specific target material, after hybridization therewith a control signal indicative is interrogated, while the control probes of the present claims do not need any control specific target material and hybridization therewith.

The response to Applicants arguments over Fodor, as set forth above, applies equally to the present grounds of rejection. Kincaid discloses control probes that comprise a sequence of nucleic acids unique to the control probe (abstract). This has been interpreted as meaning that the control probe is different than the target probe. This meets the limitations of claim 11 because claim 11 recites that the controls probes can be arbitrary sequences, meaning that the control probes are comprised of random nucleotides and are different than the target probes which are comprised of specific nucleotides for detecting the point mutations. Regarding the additional arguments that that Kincaid fails to show certain features of applicant's invention, it is noted that the

features upon which applicant relies (i.e., probes that are mixed with the target and probes that do not need any control specific target materials and hybridization) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding the rejection made under 35 USC 103 over Vernet in view of Liu the Applicants state that the claims require a microarray that includes target probes for the nucleotide sequences of point mutations at codons 528, 529, and 514 in domain B, and at codons 552, 548, and 555 in domain C, and/or codons 528 and 529 in domain B and at codon 555 in domain C. The Applicants assert that Liu does not teach that codon 529 includes a mutation. Rather, the only information concerning codon 529 in Table 2 of Liu is that "A" is the consensus wild type sequence at this position. Thus, even if Vemet and Liu were properly combined to make the present rejection (which Applicants does not admit), the combination of these references does not teach or suggest a required element of the present claims: a microarray including a probe having a mutation in codon 529.

This argument has been fully considered but is not persuasive because Liu does in fact teach a drug resistant mutation at codon 529 in Table 2. Specifically Liu teaches that HBV pol genotypes E and G have drug resistant mutations at codon 529. The wild type aa sequence has a “T” at position 529, whereas the drug resistant aa sequence has an “S” at position 529.

Regarding the rejection made under 35 USC 103 over Vernet in view of Liu and in further view of Anderson the Applicants reiterate their arguments over Vernet in view of Liu. With respect to Anderson they state that the quality-control probes described in Anderson are different from the claimed negative control probes, which are not for quality-control, of the present invention. Further, the state that Anderson discloses probes for SNPs, one is the complement of the wild type sequence and the other is the complement of the mutant type sequence. However, the probes for SNPs of Anderson are target probes regardless of whether they are wild or mutant type. In contrast, the negative control probes of the present invention are different from the target probes. As described in the specification (page 11) “in the present invention, in addition to the target probes having nucleotide sequences with which a wild type and a mutant in a codon of a target gene can be detected, negative control probes are constructed by modifying at least one nucleotide of the nucleotide sequence of each of the target probes using a method such as substitution, insertion, deletion, etc. not to be hybridized with target products."

The response to Applicants arguments over Vernet in view of Liu, as set forth above, applies equally to the present grounds of rejection. Further the argument that the probes described Anderson is different from the probes of the present invention is not persuasive. The claims require probes that have been prepared by substituting, inserting, or deleting at least one nucleotide sequence among the nucleotide sequences of the target probes not to be hybridized with a target product. Anderson teaches that for single base changes (such as a SNP) one probe was made to be the complement of

the wild type sequence, one probe was made to be the complement of the mutated sequence, and one probe was made to be the complement of a different mutation (para 0064). Therefore Anderson teaches all of the limitations of the claims. The fact that Anderson calls these "quality control probes" and the claims are drawn to "negative control probes" is irrelevant because the probes are structurally the same.

Regarding the rejection made under 35 USC 103 over Vernet in view of Liu and Anderson and in further view of Kincaid the Applicants argue that none of the cited references alone or in combination teach a probe including a mutation in codon 529 of domain B. This argument has been fully considered but is not persuasive because Liu does in fact teach a drug resistant mutation at codon 529 in Table 2. Specifically Liu teaches that HBV pol genotypes E and G have drug resistant mutations at codon 529. The wild type aa sequence has a “T” at position 529, whereas the drug resistant aa sequence has an “S” at position 529. For this reason the art rejections have been maintained.

Conclusion

11. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
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/Carla Myers/
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